

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning at page 5, paragraph 2 of the instant specification with the following paragraph:

Gene expression levels are used according to this invention to assess the progression of HPV infection from benign to malignant growth. HPV infection progresses from CIN I through CIN III and finally to malignant cancer. These stages can be identified by the ratios of HPV genes. In particular, the transition from CIN I to CIN II/III, i.e., a transition to pre-malignancy, can be predicted when the ratio of the present invention exceeds one. A ratio of greater than 3 in the present invention indicates a transition from pre-malignancy to malignant cancer. Thus, a ratio below 1 indicates a low-level of CIN in an HPV infected cell. A ratio between one and about three indicates a high-grade CIN (i.e., CIN III) or pre-malignant condition. And a ratio of over about three is an indication of an HPV induced malignancy.

Please amend the paragraph beginning at page 23, line 11 to page 24, line 2, with the following paragraph:

The RNA analysis was done according to Example 1 or the following procedure. Single stranded, biotinylated, DNA probes containing the specific HPV16 gene sequences were prepared. For HaCaT and SiHa cell lines, cells were grown to confluence, cells were harvested, and the total RNA was isolated and purified using the RNEASY® kit (Qiagen Inc., Santa Clarita, CA). For W12, whole cells were used for analysis. RNA calibrators containing the complete HPV genome were prepared by transcribing (+) sense RNA from a plasmid containing the complete HPV16 genome with T7 RNA polymerase. The RNA was then diluted to 10^3 , 10^4 , 10^5 , 10^6 , and 10^7 copies per 50 μ l. Aliquots of cellular RNA were diluted to 50 μ l and then 50 μ l of Probe mix (containing the biotinylated, single-stranded DNA probe) was added and hybridized to the RNA specimens for 2 hours at 65 °. The hybridization reactions were transferred to a streptavidin coated microplate and 25 μ l of Detection Reagent 1 was added to each well. (Detection Reagent 1 contains the alkaline-phosphatase – anti-RNA:DNA monoclonal antibody conjugate.) During a 1 hour incubation with shaking, RNA:DNA hybrids were captured onto the streptavidin coated plate and were simultaneously reacted with the anti-hybrid antibody

conjugate. After several wash steps, a chemiluminescent substrate (Tropix CDP-STAR® with Emerald) was added to the wells, and the light output was measured in a microplate luminometer after 30 minutes incubation at room temperature.